WEBINAR: Changing How Researchers Think about MRI: Utilizing a simple to use, compact, MRI system to transform preclinical imaging

Questions and answers from the February 13, 2019 webinar titled "Changing How Researchers Think about MRI: Utilizing a simple to use, compact, MRI system to transform preclinical imaging"

This document includes questions we received and answered during the webinar, as well as those that we did not have time to address. Questions have been grouped into relevant categories.

M-Series System

1. **What are the advantages of using MRI compared to other imaging modalities such as ultrasound and optical imaging?**

   As mentioned during the webinar, MRI has, for a long time, been considered the gold standard in soft tissue imaging; however, the perception has been that MRI is unattainable for many researchers, requiring a specialized understanding of physics to operate.
   The M-series systems have been designed specifically to allow the pre-clinical researcher, without a background in MR physics, to be able to operate these systems allowing them to acquire quality images and to obtain quantifiable results.

   MRI does not suffer from the depth of penetration issues that may be experienced with ultrasound imaging, especially when using high-frequency sound which is often done to improve resolution on small animal imaging subjects. MRI is not limited in the structures which can be imaged, while ultrasound cannot penetrate through bone or air as is found in the skull, lungs, and intestinal tract.

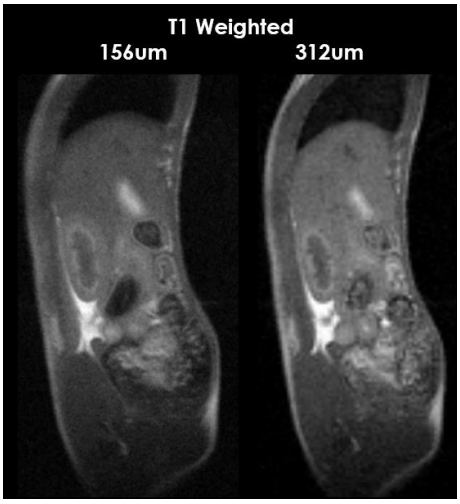
   When compared to optical imaging the resolution and anatomical structures that can be visualized using MRI provide exquisite detail, and accurate volumes can be obtained.

The Vivo-Fuse add-on can be used to co-register the optical and MR images providing anatomical reference to the molecular and functional information.

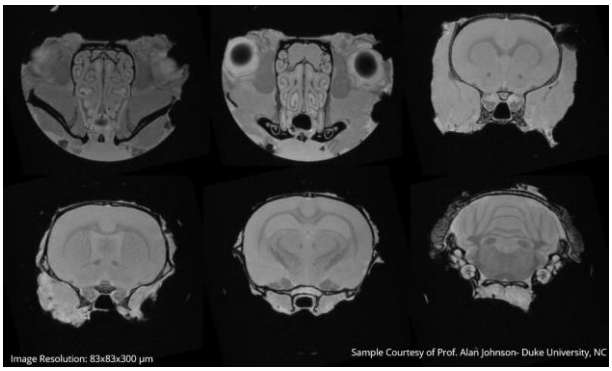
2. What is the resolution of these systems?

As with all MRI systems the resolution of the systems depends on many acquisition parameters and is therefore variable. The most important determinants of the resolution is the desired signal to noise ratio and acquisition time. The resolution should be selected which is required to answer the biological question being asked, while balancing the acquisition time.

During the presentation a slide was shown comparing images with varying resolution, signal to noise, and resulting acquisition times. For example, a 156µm resolution image took 11:07min:sec, while a 312µm resolution image took 2:30min:sec. These were whole body images that could be used to quantify volumes of a variety of anatomical or pathological structures.



The highest resolution image shown during the webinar had a resolution of 83x83x300µm resolution with a very high signal to noise ratio; that series of images of the *ex vivo* rat brain took 2 hours to acquire the entire 3D volume of the head; this image was acquired on a formalin fixed sample where acquisition time was of little concern to the animal's well-being.



To date, the highest resolution images that have been attempted have been 50x50x200µm; these images took approximately 2 hours to acquire and produced very good results. Images with 100µm isotropic resolution have been acquired in 2 hours, again with good results.

3. **Is the Acquisition Time on your images per slice or for the full scan period?**

   All of the acquisition times shown in the presentation and discussed above refer to the full scan period. Sufficient slices were acquired to cover the whole anatomical structure in all images with the exception of the cardiac images which were a single slice cineloop acquisition.

4. **How dose respiratory gating increase image acquisition time?**

   Respiratory gating will increase acquisition time; the amount of increase will depend on the respiration rate of the animal and the settings used for the gating.

   The physiological monitoring software will set up a suggested gating interval, however the user should optimize the acquisition of data between each breath to minimize the down time between each breath.

   When operating at 1 Tesla, as the M-Series systems do, the respiratory motion artefact is minimal compared to higher field systems. In fact, for most (if not all) images shown in the webinar, no respiratory gating was used and the quality of the images was not negatively affected.

5. **Is it possible to apply deep brain stimulation (electrical stimulation) in the brain with Teflon MRI-compatible electrodes and monitor fMRI with the M-series?**

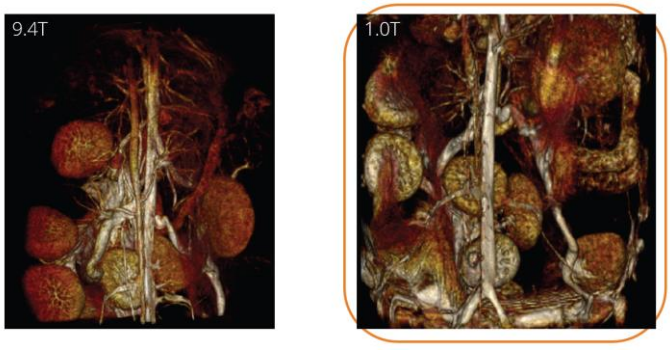
   Any MRI-compatible electrodes or devices can be used within the M-series systems, as long as the size is not prohibitive. There is an access channel through the animal handling system which allows for wires,

   cannulas and other connections to pass to the external portion of the device.

   However, functional MRI is best performed using high-field MRI. A more detailed discussion of the exact outcome that you are hoping to image may help to understand better if the M-series would be suitable or not for the specific application in this case.

6. **What would be the best MRI system to study gestation in mice, placentation, and uterine angiography during pregnancy?**

   Although not shown in the webinar today, the group at Texas Children's Hospital using the M-series systems have been doing some amazing work on rats. They are looking at gestation as well as the vasculature within the developing placenta, using a Gadolinium based contrast agent. The M-series images rival that possible with their 9.4T system, which they have open access to. Recently all of their work has moved to the M-Series system due to its ease of use and increased sensitivity to the contrast agent.



7. **What is the format of the images? Is it a standard format or does it need to be converted to another?**

   The images are acquired with the acquisition software on the workstation, however the data can be exported in any number of

   formats including DICOM, binary and raw data. Analysis software is included with the system, called VivoQuant, which works with almost all imaging systems available on the market.

8. **If the PET insert is installed, can the MRI system operate even if the insert is not functional?**

   Yes. With the PET insert installed the user can choose to acquire only an MRI image, they may also choose to acquire only a PET image if this meets their needs. The two imaging modalities operate independently of one another, however both images may be acquired simultaneously and co-registered with one another of course.

   For those who may already have a conventional MRI system, the SimPET insert can also be configured to work within these systems. Please reach out for additional information if this is the situation.

High-Field vs. Low-Field

9. **You may have mentioned this, but what is the field strength of the systems?**

   The M-series systems operate at 1 Tesla.

10. **What is the main disadvantage of low-field MRI compared to a high-field system? Can low-field MRI also perform like diffusion tensor imaging or fMRI?**

    As mentioned in the webinar the laws of physics dictate that signal to noise will always be better, with the same acquisition parameters, at high-field than at low-field. However there are several variables here including acquisition time, resolution, as well as coil and system design. As discussed above, the acquisition time and resolution of

the images should be selected to obtain the necessary image quality to answer the biological question being asked, which often does not require the signal to noise ratio seen on some high-field MR images. A lot of work has gone into the coil design for the M-series systems, as well as optimization of the electronics, to ensure the highest quality images are being acquired at all times.

Despite all of the optimization on the M-series systems, there are some applications that are not possible at 1 Tesla. Diffusion Weighted Imaging (DWI) IS possible on the M-series systems, however Diffusion Tensor Imaging (DTI) and functional MRI (fMRI) are best done at high-field strength.

Application Specific

11. **We have a chemistry group which is working on contrast agent development for MRI. However, they hope their agents will translate to human MRI. Will the low field versus high field formats be limiting for development of translatable contrast agents?**

    It would be interesting to understand if the agents being developed are Gadolinium based (or other T1 agents) or Iron Oxide based (or other T2 agents). In either case, the translation to the clinic should not be negatively affected by development at 1 Tesla compared to higher field systems. This is because of the increased sensitivity to Gd contrast agents at 1 Tesla compared to higher field systems. Although not mentioned in the webinar, the M-series systems can also be used to detect iron oxide based agents as well.

    In the clinic, typical field strengths are between 1.5 to 3 Tesla, so they are not that different than the M-series systems. As field strength increases the contrast agents interact with the protons in a similar manner, however the sensitivity to the contrast agents will only decrease as the field strength increases, specifically for Gd based agents.

12. Is Arterial Spin Labelling (ASL) something this equipment can do?

Yes, the M-series has a flow-sensitive alternating inversion recovery (FAIR) sequence which has been used to perform arterial spin labelling studies:

> Do, QN, AJ Madhuranthakam, P Bendel, RE Lenkinski. *Quantification of Mouse Renal Perfusion Using Arterial Spin Labeled MRI at 1T*. Acad Radiol. 2017 Sep; 24(9): 1079-1085.

13. How does Cineloop imaging work?

Cine is obtained by repeatedly imaging the heart at single slice location throughout the cardiac cycle. The base pulse sequence is a fast gradient echo technique triggered with ECG where every image represents a different point within the cardiac cycle.

14. Does *ex vivo* histology use small samples vs the whole animal? So the imaging core is flexible?

The MR-Based Histology add-on, which allows for automated sample handling, does use a specific sample vial to contain the specimen. These vials have soft tabs within them to help position and hold the sample in the center for optimal imaging, and slice planning. The vials have an inner diameter of 20mm and a length of 40mm.

Other sized samples can be accommodated using the available coils, (i.e. head or body coils) and sequences can be adjusted to acquire very high resolution images over prolonged acquisition times when compared to typical *in vivo* acquisitions.

Whole animal samples could simply be placed on the animal bed, without the anesthesia system turned on, to allow them to be imaged for prolonged periods of time to acquire very high resolution images.

Data Analysis

15. **How were the volumes quantified that you showed throughout the presentation?**

    The volumes shown throughout the webinar were generated using the VivoQuant software. This analysis software is included with the system. The analysis software most often is installed on a separate computer to allow analysis to be done offline and back in your office, saving time on the system for image acquisition.

    Basic visualization and analysis tools exist within the acquisition software to allow for some preliminary assessment of the images as they are acquired. VivoQuant has a variety of segmentation tools allowing for manual, semi-automated, or automatic segmentation.

Cost

16. **What is the cost for the M-series (for rats)?**

    As mentioned in the webinar the cost of a basic M3 system for mice is $290,000 USD; while an M7 system for mice and rats is $390,000 USD.
    Please reach out to us for additional information on available configurations to ensure the appropriate beds, coils and add-ons are included.